any definite effect could be expected, we feel justified in excluding them in estimating our results. Granting this, there are 35 cases in which the treatment was continued over a reasonable period of time; of these, 19 are well and 16 improved. Of the improved cases, 7 are still under treatment. Our results also varied according to the nature of the tissue diseased. Tuberculosis of the soft parts responded more readily than those in which bones or joints were involved.

Of the 28 cases previously reported by Cashman, 11 were discharged as well and 11 improved, the remaining 6 being unclassified Including these 28 cases with out present series the tuberculin dosage has been obtained and the injections made by this method in 68 cases of surgical tuberculosis. Excluding the 11 cases which have been lost sight of we have 57 cases in which the treatment has extended over a reasonable period of time; of these 57 cases, 30 were discharged as well and 27 improved.

A series of 57 cases of surgical tuberculosis, even though they have been carefully followed, is perhaps too small to allow one to draw any definite conclusions. Nevertheless, in working with this number of cases for a period of more than four years one inevitably receives very definite impressions, and we have no hesitation in declaring that the impressions gained by us have been very favorable. As stated above, our operative work in this field has been greatly reduced, and we think replaced by a much improved therapy. We strongly urge a careful unbiased trial of the method upon those men whose work carries them into this field. These cases have been observed and treated in the surgical clinic of the University of Pittsburgh, and the thanks of the writer are due and gladly given numerous colleagues for help and encouragement.

THE RELATION OF THE RECENT EPIDEMIC OF RESPIRATORY DISEASES IN DENVER TO PULMONARY TUBERCULOSIS.[1]

By James J. Waring, M.D.,
DENVER, COLORADO.

There have been under my continuous observation since November 1, 1915, 120 patients with pulmonary tuberculosis, of whom 20 were classified as incipient cases, 42 moderately advanced, and 58 far advanced. Of the first class, 2; of the second class, 9; of the third class, 12 contracted the prevailing respiratory infection, epidemic during the past winter.

The 2 incipient cases recovered completely without any sequelæ.

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[1] Read before the Medical Society of the City and County of Denver, Colorado.

Of the 9 moderately advanced cases in 3 and of the 12 advanced cases in 5 there resulted an extension of their tuberculosis. Of the moderately advanced cases, 1 exhibited, four weeks after the onset of "la grippe," an albuminuria with granular and cellular casts, which condition was not present before. Of the far-advanced cases 3 present similar urinary findings without there having been previous evidence of renal disease; 1 far-advanced patient with albuminuria progressed favorably for about five days after the onset of his new infection, and then developed complete suppression of urine for thirty-six hours, and death followed in five days. I am satisfied that this new infection precipitated the functional collapse of his kidneys. One case with severe laryngitis and tracheitis now shows a definite tuberculous laryngitis.

This is a brief summary of the cases of tuberculosis complicated by "la grippe" which I have handled in the last three months, with a note of their complications.

The pathological investigations of Cornet, Babes, Evans, Schutz, Prudden and many others long ago demonstrated secondary invaders in the walls of cavities, even in miliary tubercles far removed from the original focus of infection. There followed the isolation and identification of these germs by the method first suggested by Koch, later applied by Kitasato, and now considerably modified and improved, namely, the washing of the sputum and the taking of cultures therefrom. Inoculation of laboratory animals with cultures taken antemortem and postmortem determined their virulence. Finally, the therapeutic test of vaccine therapy and the demonstration of immune bodies in the serum add other chapters to the story of mixed infection.

It is generally accepted that secondary infection in pulmonary tuberculosis does occur, and is serious, in spite of certain negative laboratory evidence, such as the occasional demonstrated avirulence of sputum isolated organisms and the curious anomaly in the field of comparative pathology, namely, that cavity formation is rare in animals with the exception of monkeys.

During or shortly after an attack of "la grippe" the physical examination may reveal apparently an alarming extension of the tuberculous process; however, the amount of damage often cannot be determined until some weeks have elapsed after the onset of the complication. Such a case I saw recently. A young woman returning from a visit home, contracted "la grippe" en route. Physical examination indicated a widespread involvement of the left lung from apex to base front and back and in the upper and middle lobes of the right lung. Two weeks later her chest returned to the condition presented three months previously: moisture in front on the left to the third rib only and half-way to the angle of the scapula behind; on the right, moisture to be heard only in upper lobe and interscapular region behind.

Granted that shortly after a severe attack of "la grippe" a consolidated lung rapidly disintegrates, that a comparatively slight infiltration becomes more extensive, and where a month ago there were slight changes in the breath sounds and fine and medium moist rales, today there are bronchovesicular breathing and large and medium moist rales, and instead of a symptomless, retrograde process, an actively, even rapidly advancing disease with all the evidences of marked constitutional disturbance; granted all these, what are the intimate details of the transformation? What chemically and biologically happens when simple caseation passes into excavation?

In the past year the work of Jobling and Petersen[2] upon the antiferments has thrown much light upon this question, and is worthy of brief consideration. In acute caseous pneumonia a large catarrhal exudate rapidly becomes caseous, with the death of many cells known to contain ferments, and yet no autolysis takes place. Jobling and Petersen contend that secondary infection results in softening because of the entrance of fresh ferments with the new invaders, and because the body fluids necessarily accompanying the new inflammatory condition dilute the ferment inhibiting substance and aid in its removal. They have shown that lipoids containing unsaturated carbon atoms are antitryptic in colloidal solution; that tubercle bacilli and tuberculous caseous material contain such lipoids; that the reluctance of caseous material to solution and absorption is due to the presence of these compounds; that the inhibitory effect of the antiferments is overcome when the unsaturated bonds are oxydized or satisfied with iodin. This work, in addition, gives a rational chemical explanation for the solvent effect of iodin on tuberculous and luetic tissue, and forms the basis, further, for a new theory of the origin of anaphylotoxin.

The organisms chiefly incriminated in this role of secondary invader have been the influenza bacillus, pneumococcus, streptococcus, and Micrococcus catarrhalis. The investigations as to the etiology of the current epidemic of respiratory infection in Chicago by George Mathers[3] would indicate that a hemolytic streptococcus was the causal agent. Williams and Burdick,[4] in Denver, have also demonstrated a streptococcus, and by most instructive work have proved the selective tissue affinity of the organism isolated.

John Ceconi,[5] medical inspector in the Division of Communicable Diseases of the Boston Health Department, has called attention to the great need of research along biological lines in epidemic respiratory diseases. He considers the influenza bacillus the etiological agent in the recent epidemic, although admitting the great difficulty in determining finally the causative organism from inoculated plates, upon which may be found more or less numerous colonies of other pathogenic organisms, such as the staphylococcus, streptococcus, and pneumococcus.

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[2] Jour. Am. Med. Assn., 1914, lxiii, 1930. Jour. Exper. Med., 1914, xix, 251, 383, 459, and 239; ibid., 1914, xx, 321.

[3] Jour. Am. Med. Assn., 1916, lxvi, 30.

[4] Med. Record, 1916, p. 876.

[5] Boston Med. and Surg. Jour., 1916, clxxiv, 423.

Luetscher[6] has not experienced this difficulty. After establishing proper conditions for collection of sputum for examination, he says: "It will be found that in acute conditions remarkable plates will result, and that, as a rule, one organism will be present practically in pure culture." It must be added that Luetscher's work related to non-tuberculous invalids and to non-epidemic infections.

Williams and Burdick[7] isolated a hemolytic streptococcus from the sputa of patients, demonstrated complement-deviation bodies in the serum, and finally inoculated an emulsion of this germ into the ear veins of rabbits. The rabbits killed forty-eight hours later showed definite tracheitis, laryngitis, and bronchitis.

There is not only disagreement over the nature of the recent epidemic, but there are conflicting reports from bacteriologists over the prevalence of certain organisms in the sputum and the relation of these organisms to the attendant respiratory infection—whether that infection be epidemic or non-epidemic in type. For instance, Lord[8] found the influenza bacillus in pure culture in 30 per cent. of his cases of lung infection in the interepidemic period. Luetscher considers the same organism, next to the pneumococcus, one of the most important infectious agents found in pulmonary lesions. "That it is not only present in pandemics and epidemics, but also the cause of approximately 30 per cent. of the pulmonary lesions in interepidemic periods."

Williams and Burdick, in a personal communication, state that during the past two years in over 500 sputum examinations, using human blood-agar as a medium, they have failed to secure a growth of the influenza bacillus in every instance. During this time the bacillus was grown only twice—once from material obtained from the submucosa of a case of atrophic rhinitis and once from a case of Ludwig's angina. They discovered the pneumococcus only nine times. Williams and Burdick classify the *Streptococcus mucosus* as a streptococcus, a classification which is not generally accepted. Hanes,[9] concludes that Schottmuller's *Streptococcus mucosus* is really a variety of pneumococcus. Its cultural characteristics, solubility in solutions of bile salts and its behavior in comparative complement-fixation experiments all support this opinion. Luetscher[10] found the pneumococcus the cause of 62.44 per cent. of all the non-tuberculous infections below the larynx, and together with the influenza bacillus, the cause of 90.91 per cent. of the infections of the bronchi and lungs, 74.96 per cent. of the infections of the larynx and 31.29 per cent. of the infections of the nose, throat, and sinuses.

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[6] Arch. Int. Med., 1915, xvi, 657.

[7] Loc. cit.

[8] Boston Med. and Surg. Jour., 1902, cxlvii, 662; ibid., 1905, clii, 537 and 574.

[9] Journal of Experimental Medicine, 1914, xix, 38.

[10] Loc. cit.

Cecil,[11] in a bacteriological study of infections of the upper respiratory tract, recognized the streptococcus viridans as the predominant organism in 56.2 per cent. of 89 cases non-epidemic in type.

It appears therefore that Ceconi, in Boston, determined the influenza bacillus to be the cause of the recent epidemic, while Williams and Burdick, in Denver, simultaneously found the influenza bacillus not a single time.

The consumptive is particularly liable to become infected during an epidemic, among other reasons because of mouth-breathing. This habit may have been contracted in childhood from adenoids or in later life from decreased lung capacity, nasal deformity, toxemia, fever, myocardial insufficiency, distorted mediastinum, or acidosis. In this connection it is interesting to note that Yandell Henderson,[12] of Yale, suggests as a test for acidosis the length of time the breath can be held More than once we have all been impressed by the fact that in advanced pulmonary tuberculosis, usually of the fibroid type, the patient is utterly unable to hold the breath. Occasionally a patient will have hyperpnea apparently out of all proportion to the lung involvement. Such a case will almost surely have a marked acidosis, whether this be due to a heart or kidney complication or to simple pulmonary tuberculosis, with or without reference to altitude. We may safely conclude that the tuberculous individual is prone to breathe through the mouth when from exerton there is unconsciously a need for more oxygen. Moreover, there is a manifest tendency to catarrhal inflammation not only of the entire respiratory tract but also throughout the alimentary canal. The consumptive, is in addition, a physical incompetent. The very first symptom of the disease perhaps was exhaustion. Fatigue and susceptibility to infection go hand in hand. An unpublished observation of Wade Oliver, of the Pathological Institute of the Cincinnati General Hospital, quoted by Woolley,[13] is that the blood taken from the veins of patients who were brought to the hospital in a state of fatigue, such, for instance, as following a debauch, is apt to show large numbers of organisms, especially those belonging to the group of hemolytic streptococci. Oliver thinks their source is in the pyorrheic gingivitides from which most of these individuals suffer. As the physical condition of the patients improves the blood becomes sterile. It has been shown, however, that the streptococcus viridans is the organism chiefly responsible in chronic and the hemolyticus in acute infections of gums.

There is good experimental evidence to support the view that the tuberculous patient has a specifically lowered resistance to the streptococcus and staphylococcus. Sakagami[14] reveals the interesting fact that the serum of tuberculous individuals has less bactericidal power on these organisms than normal serum.

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[11] Arch. Int. Med., 1915, xv, 150.

[12] Jour. Am. Med. Assn., 1914, lxiv, 318.

[13] Jour. Lab. and Clin. Med., 1915, i, 45.

Inmates of sanatoria and residents of the outlying districts of the city are less resistant even than the city dwellers. From the very fact of their isolation they lack the benefits of automatic vaccination that comes from frequent exposure or even repeated slight infections. Their position is somewhat similar to that of the Indians in the North Canada woods, to whom influenza and measles are real scourges.

I know of no experiments which have demonstrated by the use of an aerial route of infection that the organism responsible for the recent epidemic has a selective tissue affinity for the respiratory tract. Nevertheless, granted such a portal of entry, the habit of mouth-breathing, permitting the entrance of germs very much as the night hawk scoops in gnats, a susceptibility to catarrhal inflammation, a little exhaustion, perhaps suburban residence and long absence from exposure to the germs of mixed infection, and it is easily understood why the consumptive usually contracts "la grippe."

As a result of this complication I have recorded in the patients under my care 3 cases having a peculiar homogeneous salmon-colored sputum and marked laryngitis and tracheitis. Of these 3, 2 have cleared entirely and are as well now as before their attack. One case presents, one month later, a persistent huskiness with a definite tuberculous infiltrated larynx. It is not for me to take up the relation of simple laryngitis to tuberculous laryngitis. I will confine myself to a quotation from Lockard's[15] book on *Tuberculosis of the Nose and Throat:* "Acute laryngitis in the phthisical rarely induces the accession of local tuberculosis if the attack be promptly combated, but neglected attacks or frequent infection may, under fortuitous condition, lead to infection, or in healed lesions to a recurrence." Robert Levy, of Denver, from the wealth of his experience, has voiced repeatedly the same opinion.

Four cases not previously showing any evidence of kidney degeneration, developed during their illness a persistent albuminuria with granular and cell casts. It has long been noted that the consumptive apparently overcomes his lung trouble to die later of kidney degeneration. At any rate, we have all been impressed by the frequency of albuminuria in the moderately advanced or far-advanced cases, particularly in those who have been overfed for a long time. A patient raising daily two to four ounces of purulent sputum imposes an eliminative burden upon the kidneys which cannot be estimated, but must be very great. Barker[16] has called attention to the fact that the "toxic glomeruler nephropathies are often due to streptococcus toxins. The possibility of the complication should be thought of in every case of streptococcus sore throat, hence the general practitioner can do much in the way of prevention. *Every individual who suffers from sore throat, tonsillitis, or 'bad cold,' with fever, should be put to bed and be kept warm there until the infection is overcome.* Not only would much renal disease be thus avoided, but also many serious disorders of the heart and of the joints." Not only is it possible that the lungs may be infected secondarily by the streptococcus, either sporadically or during an epidemic, but it is extremely probable that the lung thus infected may become a focus for further metastasis to heart or kidneys. Parenthetically it may even be possible for the tuberculous lung to acquire a mixed infection from an abscess at the root of a tooth.

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[14] Lancet, 1916, i, 127.

[15] Lockard: Tuberculosis of Nose and Throat, 1909.

[16] Am. Jour. Med. Sc., 1913, cxlv, 42.

The *Bulletin* issued by the city of Philadelphia Board of Health says: "Don't forget that this disease"—la grippe—"may be complicated by pneumonia. It causes a profound depression upon the body, and is likely to affect the heart and kidneys."

Bonney,[17] in his book, *Pulmonary Tuberculosis and its Complications,* says: "There is ample clinical evidence to substantiate the belief that a prolonged secondary infection, though slight in degree, is sufficient to produce desquamative and degenerative changes in the kidneys of pulmonary invalids." Again, "Irrespective, however, of this consideration it is clearly demonstrated that kidney disturbances are much more common in those cases of pulmonary tuberculosis exhibiting varying degrees of secondary infection."

In the use of vaccines this established deleterious effect of streptococcic toxines upon the kidney must not be forgotton. In fact, the prolonged administration of any vaccine in anything but small doses may not be without considerable harm to the renal parenchyma. Longcope[18] by injecting egg albumen into animals has produced definite histological changes in the kidneys. That any anaphylactic reaction causes renal degeneration is not perhaps a warranted deduction from this work, particularly as it awaits confirmation. Nevertheless it adds one more warning against indiscriminate vaccine therapy.

The work of Travis[19] would indicate that milk proteins as such do not enter the circulation of severe cases of nephritis kept for some time on an almost exclusive milk diet. We do know that there are many cases on record of hypersensitiveness to egg proteins. The urine of patients ingesting many eggs may contain these proteins. Finally the tuberculous individual taking six to nine eggs daily and having a moderate trace of albumin, with many granular and cellular casts in the urine and losing weight, may upon the withdrawal

[17] Pulmonary Tuberculosis and its Complications, 1910.
[18] Jour. Exper. Med., 1913, xviii, 678.
[19] Annual Report of Health Officer of Port of New York, 1916.

of the eggs from his diet show a diminished quantity of albumin, fewer casts, and a corresponding symptomatic improvement.

In the absence of any specific remedy capable of routine administration in the treatment of tuberculosis, our main reliance must consist in making the patient take and assimilate a large, often a very large, amount of nourishment. From the ingestion, however, of twelve raw eggs, 84 grams of protein, one or two quarts of milk, 28 to 56 grams of protein, perhaps 3 or 4 cooked eggs, besides steak or roast beef, 40 to 60 grams of protein, together with a half-pint or more daily of extractives in the form of soup and beef juice, there should be afforded some idea as to the amount of waste nitrogenous matter the kidneys have to eliminate. Many patients compelled to take this amount of food are already laboring under a severe toxemia from the tuberculous process in the lungs, with perhaps an indolent superadded mixed infection. Given a patient so handled for six to twelve months, or longer it is not surprising there should develop an albuminuria coincidentally with an acute streptococcus infection of the upper or lower respiratory passages. I would not go on record as inveighing against forced feeding. It is invaluable at times. I am convinced, however, that a diet with two or three times the normal proteid standard continued for a long time may pave the way for the functional collapse of the kidneys at such critical times as those of acute severe mixed infection.

Time and space do not permit me to enlarge upon another very important phase of this subject—the possibility of damage to the heart. Reduction of the pulmonary vascular bed, toxemia, or distortion of the mediastinum by adhesions or other cause may severely handicap the heart in pulmonary tuberculosis. Certain it is that in acute articular rheumatism, scarlet fever, in fact in any febrile disturbance due to a streptococcic infection or associated with it, the heart may show sooner or later definite signs of myocardial degeneration. If the non-tuberculous individual should be protected against endocarditis and myocarditis when contending with a streptococcic infection, certainly the tuberculous invalid, whether we accept the theory of cardiac hypoplasia of older writers or not, is more than entitled to that same degree of protection.

Babcock[20] says: "The danger to life from such a degenerative process makes prolonged observation of the patient after convalescence from an attack of influenza highly important," and "not only is the function of the organ disturbed in the course of influenza, but signs of cardiac inadequacy may develop a considerable time afterward."

Recognizing early in November that a severe epidemic of "la grippe" was prevalent throughout the country, and feeling keenly my responsibility not only to my own patients but the many of

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[20] Osler's System of Medicine, Lea & Febiger, 1913.

Doctor Bonney's under my care, I diligently and repeatedly admonished nearly all of them not to visit the moving-picture houses, the auditorium, the theatre, and other public buildings; to avoid the department stores above all places in doing their Christmas shopping. (As many as 35 to 40 saleswomen were sent home one day from one of the larger department stores of this city, with an estimated morbidity of 50,000 cases of "la grippe" in a population of 250,000.) They were urged, as far as possible, to keep off the street cars. Many were not allowed to go into the shopping district at all. All were forbidden to visit their friends ill with "la grippe," and were told not to receive any visitor with a bad cold or any recently recovered therefrom. Every patient, tuberculous or not, who contracted "la grippe" was promptly put to bed and kept there until every vestige of the acute infection had subsided.

One word on the subject of treatment after the acute stage: Specific treatment is now the vogue—perhaps not so much as a year or two ago, but still much resorted to.

I am inclined to think that one reason why vaccine therapy in mixed infection is so frequently unavailing is that the germs of the mixed infection have become so firmly established—"dug in," so to speak, in the walls of old cavities, large or small—that even though the serum may show a large content of immune bodies they are unable to reach the germs in sufficient concentration to effect their dislodgment. The walls of these old cavities are composed of tough old scar tissue in which tissue destruction and regeneration are at low tide and blood and lymph circulation stagnant. Phagocytic cells penetrate slowly this tissue and must meet the invading germs improperly supported by immune bodies and with their activity limited, perhaps by age and certainly by their environment. The natural resistance of the tissue cell is low at the immediate point of attack. In these cases the invader acquires such resistance to the defensive powers of the host, and the latter such resistance to the harmful effect of the invader that a prolonged condition of infection ensues—what Hans Zinsser calls a "sort of truce without manifestation of disease?" until a repeated infection perhaps carries off the patient.

The great lesson of this recent epidemic is not whether the causative agent, is a streptococcus that does or does not ferment this or that carbohydrate, but that we and our patients are periodically exposed to a malady of great contagiousness, caused this year by a streptococcus, perhaps next year by a pneumococcus. At any rate, the infection is produced by a germ with whose biological characteristics we are for the most part unacquainted. When it becomes apparent that such an epidemic is upon us, stringent prophylactic measures should be instituted, including the isolation of all cases. The causative organism should be identified, following which it is important that its tissue affinity be established and serological experiments instituted, to the end that we may know, not so much what value may be placed upon curative vaccine therapy but what protection we may expect from prophylactic inoculation. We should know whether general antigrippe inoculation is feasible.

Other organisms must be studied along lines laid down by Cole[21] Dochez[22] and other workers[23 24 25] in the Rockefeller Institute in the case of the pneumococcus and by Martha Wollstein[26] in the case of the influenza bacillus.

In conclusion, in pulmonary tuberculosis "la grippe" may prove a fatal complication—the last straw that breaks the back of his resistance—by establishing in the lungs an ineradicable secondary infection with its attendant dangers—by inflicting upon him that dreaded complication, tuberculous laryngitis, by causing the collapse of already overburdened kidneys or weakened heart.

It is incumbent upon us therefore to protect to the last degree the tuberculous invalid from this epidenic form of respiratory infection.

ANALYSIS OF THIRTY CASES OF PULMONARY TUBERCULOSIS TREATED BY THE INDUCTION OF AN ARTIFICIAL PNEUMOTHORAX.[1]

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In this paper it is my intention to abstain wholly from details of technic and to present that in which after all we are most interested, the results of treatment.

It need merely be mentioned that by the induction of an artificial pneumothorax it is sought to compress the lung in an "air splint," this air splint consisting of nitrogen gas allowed to flow between the parietal and visceral layers of the pleura; and that by maintenance of this compression and consequent absolute rest to the damaged organ for a period of time varying from six months to three years it is hoped to obtain cicatrization and healing of the diseased lung. Cases suited for this treatment are either those that are wholly unilateral or those with severe involvement on one side and comparatively insignificant disease on the other.

In my work I have used exclusively the puncture method of

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[21] New York Med. Jour., 1915, ci, 1 and 59.

[22] Jour. Exper. Med., 1912, xvi, 665.

[23] Dochez and Gillespie: Jour. Am. Med. Assn., 1913, lxi, 727.

[24] Bull: Jour. Exper. Med., 1915, xxii, 457, 466 and 484.

[25] Gay and Chickering: Jour. Exper. Med., 1915, xxi, 389. Chickering: Ibid., 1915, xxii, 248.

[26] Wollstein: Jour. Exper. Med., 1915, xxii, 445.

[1] Chairman's address in the Section on Practice of Medicine, read before the North Carolina Medical Society.